

Application Number 10/521531  
Response to the Office Action dated April 1, 2010

### REMARKS

Favorable reconsideration of this application is requested in view of the following remarks.

The specification has been amended to clarify that the "supercritical water" disclosed in Tetrahedron Letters 1996, 37, 3445, which is cited in the rejection as Junk et al. (Junk I), is supercritical D<sub>2</sub>O as disclosed in Junk I at page 3445, first paragraph and further amended editorially as listed above. No new matter has been raised by the amendments to the specification.

Claim 1 has been amended as supported by the specification at page 1, lines 29-31, page 2, lines 21-25, page 25, lines 11-16, and examples 1-16 on pages 27-28 and table 1 on page 29. No new matter has been raised by the amendments to claim 1.

Claims 1-4 and 7-11 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Dinh-Nguyen et al. (U.K. Patent No. 1,103,607) or Junk et al. ("Preparative supercritical deuterium exchange in arenas and heteroarenes", Tetrahedron Letters, Vol. 37, No. 20, pp. 3445-3448, 1996) (Junk I) in view of Junk et al. (U.S. Patent No. 5,830,763) (Junk II) or Bergman et al. (U.S. Patent No. 6,794,522). Applicants respectfully traverse this rejection.

Claim 1 excludes D<sub>2</sub>O<sub>2</sub> and supercritical D<sub>2</sub>O from a deuterated solvent. Dinh-Nguyen discloses replacement of light hydrogen by deuterium by using deuterium peroxide (D<sub>2</sub>O<sub>2</sub>) as a promoter (see page 1, left coln., lines 30-45). For example, by the method of Dinh-Nguyen, deuterated compounds having high isotopic purity of over 99 % can be obtained (see page 1, right coln., lines 54-58). Thus, in order to obtain such highly deuterated compounds, inclusion of D<sub>2</sub>O<sub>2</sub>, which is excluded from claim 1, in the reaction system is essential for Dinh-Nguyen. Accordingly, claim 1 is distinguished from Dinh-Nguyen in this respect. When D<sub>2</sub>O<sub>2</sub> is used in the deuteration reaction, a substrate compound that may be decomposed with D<sub>2</sub>O<sub>2</sub> cannot be deuterated (see page 2, lines 9-

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15 of the specification). When  $D_2O_2$  is not included in the reaction system of Dinh-Nguyen, the deuteration ratios would be low (see page 1, lines 17-37 of Dinh-Nguyen). Thus, the deuteration method of claim 1 that can provide high deuteration ratios without using  $D_2O_2$  is unexpected from Dinh-Nguyen (see table 1 on page 29 of the specification). Further, because  $D_2O_2$  is an essential element for the reaction of Dinh-Nguyen in order to achieve the high deuteration ratios, there is no reasonable basis to assume that such high deuteration ratios can be achieved when  $D_2O_2$  is replaced with another deuterated solvent in the method of Dinh-Nguyen.

As discussed above, claim 1 excludes deuterium peroxide ( $D_2O_2$ ) and supercritical  $D_2O$  from the deuterated solvent and recites that the reaction is carried out under non-supercritical condition. Junk I discloses supercritical deuterium exchange (SDE), which uses deuterium oxide ( $D_2O$ ) above its triple point ( $374^\circ C$ , 221 bar), without using a metal catalyst (see first and second paras. on page 3445 and scheme 1 on page 3446). Thus, Junk I does not remedy the deficiencies of Dinh-Nguyen.

In addition, the compounds to which the SDE of Junk I is applicable are limited to those that are stable under the SDE conditions, and some compounds such as benzylic carboxylates and halogenated aromatic compounds, which are unstable under the SDE conditions, are not suitable for the SDE (see last para. on page 3446 and table 1 on page 3447). In contrast, by using the method of claim 1, the aromatic ring substituted with an alkoxycarbonyl group, for example benzylic carboxylates, and halogenated aromatic compounds can be deuterated (see page 14 lines 7-28 and table 1 on page 29 of the specification). Thus, the method of claim 1 is not as substrate specific as the method of Junk I.

Similar to Junk I, Junk II discloses a deuteration method of organic compounds under a supercritical condition using supercritical deuterium oxide ( $D_2O$ ) as the reaction medium (see abstract and coln. 2, lines 63-65). Claim 1 excludes the supercritical condition using supercritical  $D_2O$ . Accordingly, Junk II also does not remedy the deficiencies of Dinh-Nguyen and Junk I.

Bergman discloses a deuteration method of organic compounds using  $D_2O$  or a mixture of  $D_2O$  and  $CD_3CO_2D$  (see coln. 5, lines 24-28), and Bergman fails to disclose an

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activated mixed catalyst as claim 1 recites. As discussed above, for Dinh-Nguyen,  $D_2O_2$  is an essential element in order to obtain high deutration ratios (see page 1, left coln., lines 30-45), and in Dinh-Nguyen,  $D_2O_2$  is not replaceable with  $D_2O$  or a mixture of  $D_2O$  and  $CD_3CO_2D$  of Bergman. Accordingly, there is no reasonable basis to combine Dinh-Nguyen and Bergman, and this rejection should be withdrawn.

In view of the above, Applicants request reconsideration of the application in the form of a Notice of Allowance.

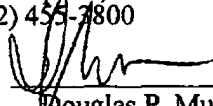


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